The Monster in the Closet

Mothballs' Link to Non-Hodgkin Lymphoma

Each year, according to the American Cancer Society, about 54,300 Americans are diagnosed with non-Hodgkin lymphoma (NHL), a cancer that originates in the lymph tissue, and about 19,400 people die from it. Several lines of evidence point to a possible association with pesticides. The incidence of NHL has roughly doubled since the 1970s, a few decades after a marked rise in U.S. household and agricultural pesticide use, and previous studies have found increases in chromosome aberrations and micronuclei in lymphocytes among pesticides applicators and some groups of farmers. This month, Ikuko Kato of Wayne State University and colleagues report an increased risk of NHL among New York State women with several types of pesticide exposure at home and on the job [***EHP* 112:1275–1281**].

In the retrospective case–control study, 376 women recruited at NHL diagnosis in the late 1990s were compared to 463 age-matched controls. Cases were identified through the New York State Cancer Registry; controls were found through the Health Care Financing Administration or state Department of Motor Vehicle records. All participants answered a survey regarding past exposure to pesticides of all types. Whereas most previous studies of the association between cancer and pesticide exposure have focused on occupational exposure, Kato and colleagues also asked about home exposure to products such as mothballs, flea and ant killers, head lice treatments, and house plant products.

The highest risk of NHL was associated with pesticide exposure that began between 1950 and 1969. The authors speculate that this relationship could reflect a long latency period for NHL, or the historic use of compounds that are particularly toxic and now banned, such as the organochlorine pesticides.

Among women who used pesticides at home, the 25% with the highest use had a 62% greater chance of developing NHL than women who never used such products. Also, NHL risk was 2.12 times greater among women who had worked at least 10 years on a farm where pesticides were used, compared with women who never worked on a farm.

When analyzing use of specific products, the researchers found a significant correlation between use of mothballs and NHL, although not a clear dose–response relationship. The authors note that the active ingredients of mothballs may be inhaled or absorbed through the skin during contact with treated clothing. Naphthalene and paradichlorobenzene, common active ingredients in mothballs, are among the most common toxic chemicals detected in indoor air. Earlier studies correlated these compounds with blood diseases including aplastic anemia and hemolytic anemia. *In vivo* and *in vitro* studies have shown cytotoxicity, genotoxicity, and carcinogenicity for naphthalene, paradichlorobenzene, and their metabolites.

The findings were limited by the possibility of recall bias—cancer patients may be more motivated than controls to remember pesticide exposure. However, a counterbalancing bias may have existed: exposed controls, upon learning that pesticides were one of the major research interests, may have been more interested in participating than nonexposed controls. Additionally, fewer than 50% of the subjects could recall the names of pesticides that had been used at their workplaces. While establishing a correlation between exposure to pesticides and disease does not prove that the pesticides caused disease, it does add detail to the growing picture of pesticide-caused hematologic toxicity, and suggests a need for further study of mothballs in particular. **–David J. Tenenbaum**

Saves clothes, not health. The naphthalene and paradichlorobenzene in mothballs may put those who use them at risk for non-Hodgkin lymphoma.

Arnold Greenwell/EHP

Arsenic and Intellectual Function

Bangladeshi Children at Risk

In Bangladesh, naturally occurring arsenic contaminates some 10 million tube wells that about 30–40 million people depend on for drinking water. Scientists have already established that adults with heavy exposure to arsenic can suffer adverse impacts on cognitive functions such as learning and memory. However, there have been no well-controlled studies of the neurological consequences of arsenic exposure in children. This month, a group of U.S. and Bangladeshi researchers led by Gail Wasserman of Columbia University provides evidence that even modest exposure to arsenic in drinking water is associated with reduced intellectual function in children in Araihazar, Bangladesh [***EHP* 112:1329–1333**].

The investigators studied a group of 201 10-year-old children. The children's parents were participating in an ongoing study of arsenic exposure among residents in a 25-square-kilometer region located about 30 kilometers east of Dhaka. The study site, Araihazar, was chosen because of its wide range of arsenic concentrations in drinking water.

The research team's earlier survey of 6,000 contiguous tube wells in the region showed concentrations in individual wells ranging from less than 1 microgram per liter (μg/L) to 900 μg/L. Of the wells surveyed, 75% exceeded the World Health Organization (WHO) arsenic standard of 10 μg/L, and 53% exceeded the Bangladeshi standard of 50 μg/L.

In the current study, children and their mothers came to the research team's field clinic for examination by a physician. The children provided urine specimens for the measurement of urinary arsenic and creatinine; about half also agreed to provide blood samples for measurement of blood lead and hemoglobin. Each child's mother provided information about the family's primary source of drinking water, and these sources were matched to the previously surveyed wells. In an effort to control for sociodemographic variables, the research team asked parents about parental age, education, and occupation, among other questions. The team also controlled for drinking water exposure to manganese, another known neurotoxicant (in their earlier survey, they had found that 82% of wells surveyed for manganese exceeded the WHO standard of 500 μg/L).

In addition to the medical evaluation, the children were assessed using an adaptation of the Wechsler Intelligence Scale for Children, version III (WISC-III). Because of the lack of standardized

IQ measures in Bangladesh, Wasserman, a child psychologist, adapted the WISC-III for this cultural context. The WISC-III is a comprehensive series of tests that measures intellectual abilities such as comprehension and problem solving. Verbal subtests together provide a Verbal IQ, and a number of performance subtests (such as Picture Completion, Coding, Block Design, and Mazes) together provide a Performance IQ.

The researchers found that consumption of water contaminated by arsenic was associated with reduced intellectual function in a dose–response fashion. Children with exposures above 50 µg/L had significantly lower Performance and Full Scale scores than children with exposures under 5.5 µg/L. The children with the highest quartile of water arsenic also had marginally reduced Verbal scores. Lead and manganese exposures were not conclusively associated with impaired intellectual function, likely due to the low number of blood samples and confounding between arsenic and manganese, respectively.

The research team is working to curb exposure to arsenic in the study region. Since arriving in 2000, U.S. researchers, along with Bangladeshi colleagues, have overseen the installation of low-arsenic private and community wells and implemented a village education program that has successfully reduced some exposure. The authors note that the associations between arsenic and intellectual function were stronger for well-water concentrations than for urinary concentrations, which reflect recent exposure. The urinary concentrations at the time of testing may not reflect the full magnitude of the children's earlier exposure, and the authors write that recently reduced exposure may explain the weaker associations between intellectual function and urine arsenic, compared to well-water arsenic. **–John Tibbetts**

Aflatoxin Exposure after Weaning

Solid Food Contaminant Impairs Growth

Given the heat, humidity, and poor storage conditions of many tropical developing nations, mold readily grows in harvested crops such as maize and groundnuts. Such foods are dietary staples in many of these countries, and their consumption can lead to widespread exposure to aflatoxin, a mold toxin produced by *Aspergillus* species that is known to cause liver cancer. Aflatoxin is also associated with impaired growth and immune function in animals, but minimal data exist regarding comparable effects in humans. To examine a potential link more closely, a team of researchers in the United Kingdom and Benin built upon an earlier cross-sectional study that demonstrated impaired growth among West African children with high aflatoxin exposure [***EHP* 112:1334–1338**]. The researchers now present evidence from a longitudinal study that aflatoxin does impair growth in humans.

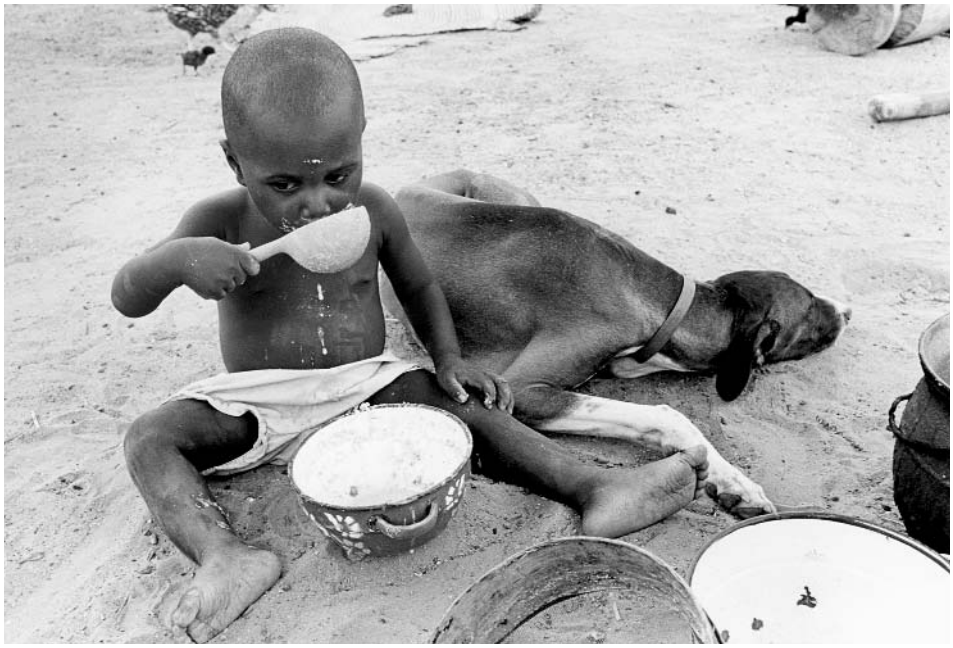
Previous studies indicated that aflatoxin exposure is high in West African populations, and dietary exposure begins with the introduction of solid foods at weaning. Maize, in the form of porridge, is often the first solid food given to young children here. To study the effects on growth of probable aflatoxin exposure at a young age, the team recruited 50 children from each of four villages in the West African nation of Benin. The children were 16–37 months old when the study began in February 2001. The children's mothers were interviewed in February, June, and October to gather information about each child's diet, health, and other factors. Blood samples collected from the children at each survey point were analyzed for levels of aflatoxin–albumin, a biomarker of recent aflatoxin exposure. Vitamin A and zinc levels also were obtained as markers of nutrition. The children and their mothers were weighed and measured at each survey point.

At the first survey point, the researchers found that levels of aflatoxin–albumin were significantly higher in weaned children than in those still partially breastfeeding. Throughout the study, more children became fully weaned, and the levels of the biomarker increased in these children. More than 98% of the children were positive for aflatoxin–albumin at all three time points. Most exposure was likely due to maize consumption, although eating other foods such as groundnuts may have contributed.

Children with the highest levels of the aflatoxin biomarker grew an average 1.7 centimeters less than those with the lowest levels. Poor nutrition did not appear to be a factor in the reduced growth, as blood concentrations of vitamin A and zinc were not correlated with aflatoxin–albumin levels.

The mechanism by which aflatoxin could affect growth is currently being investigated. Defining aflatoxin's effects is complicated by confounding dietary variables (including co-contamination of food with additional mycotoxins) and the presence of infection. For example, previous research by this group revealed an association between aflatoxin exposure and reduced levels of protective antibodies in the saliva of Gambian children. The team therefore theorizes that aflatoxin could affect growth by altering mucosal barriers and lowering resistance to intestinal infection.

The group is now conducting research aimed at better understanding such relationships. They suggest that controlling for many confounding factors will require a randomized intervention study in which aflatoxin exposure would be reduced to assess the toxin's impact on children's immunity, growth, and disease susceptibility. **–Julia R. Barrett**



Trygve Bolstad/Panos Pictures

A somber start. Maize porridge—a potential source of growth-limiting aflatoxin exposure—is often the first solid food given to West African children such as this boy in Burkina Faso.